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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/588,689	06/29/2007	Ryan Smith Westberry	186257/US	9609

80964 7590 09/29/2009

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EXAMINER	
KIM, YOUNG J	

ART UNIT	PAPER NUMBER
1637	

MAIL DATE	DELIVERY MODE
09/29/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/588,689	WESTBERRY ET AL.	
	Examiner	Art Unit	
	Young J. Kim	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 July 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 19-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14 and 19-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 24, 2009 has been entered.

Preliminary Remark

Claims 15-18 are canceled.

Claims 24-31 are new.

Claim Duplication Warning

Applicant is advised that should claims 1-10, 20, and 21 be found allowable, claims 31, 2-10, 20, and 21 will be objected to[1] under 37 CFR 1.75 as being a substantial duplicate thereof.

Claims 2-10, 20, and 21 are multiple dependent claims, each of which depends from either claim 1 or 31.

Claims 1 and 31 are both drawn to a product, whose metes and bounds are solely defined by its physical attributes (and not based on their intent of use).

Claims 1 and 31 have identical set of regents comprised by a reaction mixture, that is - a) each conventional nucleotide dATP, dCTP, dGTP, and dTTP in combination with dUTP as a replacement for a portion of dTTP, wherein said dUTP replaces from about 10 to about 50% of said dTTP in said reaction mixture; and b) at least one of a fluorescent probe, beacon, or intercalating dye.

While claim 31 recites that the mixture is, "[a]n improved reaction mixture," the actual mixture contains the same set of reagents that that of claim 1. Therefore, the claims are deemed duplicates of each other. Claims 2-10, 20, and 21 are each dependent on claims 1 and 31 and thus are also identical in scope (i.e., duplicates).

Applicant is advised that should claims 11, 13, 19, and 24-30 be found allowable, claims 12, and 22-30 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof.

Claims 24-30 are multiple dependent claims, each of which depends from claims 11 and 12.

Claims 11 and 12 are duplicates because they require the same set of steps, embracing the same scope, although the wording may vary slightly.

Claims 13 and 19 corresponds to claims 22 and 23.

When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Correction is required.

Drawings

Applicants' amendment received on June 26, 2009, amending to specification to comply with the sequence rules set forth in 37 CFR 1.821-1.825 is noted. The objection to the specification noted in the Office Action mailed on February 26, 2009 has been withdrawn therefore.

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[1] Claims 2-10, 20, and 21 are multiple dependent claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-14 and 19-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 12 and 31 are identical to claims 11 and 1 (respectively). It is unclear what the improvement is therefore. In addition, if the claims are intending to follow Jepson format, then the format of claims 12 and 31 are improper as required under 37 CFR 1.75(e).

Claim is indefinite for reciting the phrase, "wherein said dUTP replaces from about 10 to about 50% of said dTTP in said reaction mixture for the following reasons."

Since the claim does not recite how much of dTTP was present, it cannot be determined how much dUTP constitutes a 10-50% replacement of the dTTP which was originally present.

For example, if a mixture contains 100 mM dTTP and 100 mM of dUTP, wherein some unknown original amount of dTTP was 200 mM dTTP, then the dUTP would have replaced 50% of the dTTP. However, if the original amount of dTTP was 100 mM, then dUTP would have not replaced any of the dTTP, even though the both reaction mixture contains the same amount of dTTP and dUTP (100 mM each).

For the purpose of prosecution, the phrase has been construed to mean, "said dUTP is at about 10 to about 50% of the dTTP in said reaction mixture."

All pending claims are indefinite analogously.

Correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 3, 7-12, 24, 25, and 27-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Bohlander, S.K. (U.S. Patent No. 5,731,171, issued March 24, 1998).

Bohlander discloses a regent composition comprising:

each of dATP, dCTP, dGTP, and dTTP ("following conditions: … 150 uM each dATP, dGTP, and dCTP, 110 uM dTTP…) in combination with dUTP ("… 40 uM Bio-11-dUTP…"), wherein said dUTP is at about 10 to 50% of dTTP (40/110 = 37% of dTTP is dUTP), wherein said mixture comprises a fluorescent probe, beacon or intercalating dye ("products may also be labeled with the fluorophore Spectrum-Orange" column 20, lines 59-63), thereby anticipating claims 1 and 31.

Regarding claims 11 and 12, Bohlander detects the amplified product (see column 24, lines 33-36, hybridization against cDNA libraries on solid support).

With regard to claims 2, 3, 24, and 25 the artisans also contemplate a mixture comprising 150 uM of each dNTPs and 30 uM of dUTP, which translates to the presence of dUTP at 20% of dTTP concentration.

With regard to claims 7, 8, 27, and 28, the concentration of dUTP (40 uM or 30 uM) does not exceed 300 or 100 uM.

With regard to claims 9, 10, 29, and 30, the artisans disclose that the composition comprises a polymerase (Taq DNA polymerase, see column 20, lines 50-54), and a buffer system (Tris HCl).

Therefore, Bohlander anticipates the invention as claimed.

Claims 1-3, 5, 7-12, 24, 25, and 27-31 are rejected under 35 U.S.C. 102(a) and (e) as being anticipated by Mukai et al. (US 2003/0073081 A1, published April 17, 2003, filed August 23, 2001).

Mukai et al. disclose a reaction mixture for primer-based amplification, said reaction mixture comprising:

each conventional nucleotide dATP, dCTP, dGTP, and dTTP in combination with dUTP as a replacement for a portion of the dTTP ("A reaction mixture of total volume of …. 0.625 mM each of dATP, dCTP, and dGTP, 0.625 mM of a dTTP+Aminoallyl dUTP mixture" (section [0955]), wherein said dUTP replaces from about 10 to about 50% of said dTTP in said reaction mixture ("The ratio of amino group introduced into an ICAN amplification product was examined by changing the ratio of the amount of dTTP to the amount of Aminoallyl dUTP in the ICAN reaction as follows: 10:0, 9:1, **8:2, 7:3 and 6:4**[2]." section [0954]); and

at least one of a fluorescent probe, beacon or intercalating dye ("After electrophoresis [of the amplified product], fluorescent dye was detected using FM-BIO. Furthermore, the ICAN-amplified fragment was detected by staining with EtBr." section [0958]), thereby clearly anticipating claims 1-3 and 31.

With regard to claims 11, 12, 24, and 25, the artisans teach a method of amplifying and detecting the amplified product ("After electrophoresis [of the amplified product], fluorescent dye was detected using FM-BIO. Furthermore, the ICAN-amplified fragment was detected by staining with EtBr." section [0958])

[2] dTTP/dUTP ratio of 8:2, 7:3, and 6:4, necessarily means that 20 % of what would be dTTP (to be 100% dTTP) is dUTP. Similarly, the ratio of 7:3 would necessarily mean 30% of what would be dTTP would be dUTP; and the ratio of 6:4 would necessarily mean 40% of what would be dTTP would be dUTP.

With regard to claim 5, the artisans employ a primer pair, SEQ ID Numbers 281 and 282, which are chimeric primers comprising a combination of ribonucleotides and deoxyribonucleotides (section [0955] and "SEQ ID NO: 281:–Designed chimeric oligonucleotide primer designated as MF2N3(24). 'nucleotides 22 to 24 are ribonucleotides-other nucleotides are deoxyribonucleotides.'"; "SEQ ID NO: 282: Designed chimeric oligonucleotide primer designated as MR1N3(24). 'nucleotides 22 to 24 are ribonucleotides-other nucleotides are deoxyribonucleotides.'" sections [1250] and [1251]).

With regard to claims 7, 8, 27, and 28, the artisans disclose that the concentration of dNTPs used is 0.625 mM, and thus, dUTP concentration would not exceed about 300 uM or about 100 uM (since 9:1 ratio of dTTP:dUTP in the amount of 0.625 mM (or 625 uM) would be 62.5 uM).

With regard to claims 9, 10, 29, and 30, the reagent mixture disclosed by the artisans comprises HEPES-potassium hydroxide buffer and BcaBEST DNA polymerase (section [0955]).

Therefore, Mukai et al. clearly anticipate the invention as claimed.

Claim Rejections - 35 USC § 103

The rejection of claims 1-12 rejected under 35 U.S.C. 103(a) as being unpatentable over Danielsen et al. (WO 02/090536 A2, published November 14, 2002; IDS ref) in view of Haberhausen et al. (U.S. Patent No. 6,248,522 B1, issued June 19, 2001), made in the Office Action mailed on February 26, 2009 is withdrawn in view of the arguments/claim amendment made in the Amendment received on June 26, 2009.

The rejection of claims 13, 14, and 19-23 under 35 U.S.C. 103(a) as being unpatentable over Danielsen et al. (WO 02/090536 A2, published November 14, 2002; IDS ref) in view of

Haberhausen et al. (U.S. Patent No. 6,248,522 B1, issued June 19, 2001) as applied to claims 1-12 above, and further in view of McLaughlin et al. (U.S. Patent No. 6,783,940 B2, issued August 31, 2004, filed October 31, 2001), made in the Office Action mailed on February 26, 2009 is withdrawn in view of the Amendment received on June 26, 2009. Haberhausen et al. fails to cure the deficiency in the teachings of Danielson et al., and therefore, the rejection must fall.

Rejections, New Ground – Necessitated by Amendment

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 4, 6, 13, 14, 19-23, and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mukai et al. (US 2003/0073081 A1, published April 17, 2003, filed August 23, 2001) in view of McLaughlin et al. (U.S. Patent No. 6,783,940 B2, issued August 31, 2004, filed October 31, 2001; cited previously).

The teachings of Mukai et al. have been discussed above.

Mukai et al. do not disclose the use of mannitol or sorbitol.

McLaughlin et al. disclose that sorbitol reduces non-specific amplification in a DNA polymerase chain reaction involving sorbitol (column 2, lines 13-15), with said sorbitol concentration ranging from 0..25M to 0.35M (which is 250 mM to 350 mM, respectively; column 2, lines 25-27).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Mukai et al. with the teachings of McLaughlin et al., thereby arriving at the claimed invention for the following reasons.

As Mukai et al. demonstrate a method of amplifying a target nucleic acid sequence using PCR primers, said one of ordinary skill in the art would have been reasonably motivated to employ other reagent means which would also further aid in specific target amplification, such as that of McLaughlin et al.

In *KSR International Co. v. Teleflex Inc. (KSR)*, (citation omitted), the Supreme Court expressed that, "[t]he combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predicable results." *Id.* at __, 82 USPQ2d at 1395.

Clearly, one of ordinary skill in the art at the time the invention was made would have recognized that adding art-recognized amounts of sorbitol in an amplification reaction mixture, as evidenced by McLaughlin et al., would have resulted in the predictable result of providing higher specificity in amplification reaction.

Additionally, the MPEP, at 2143.02, states that the prior art can be modified or combined to reject claims as obvious as long as there is a reasonable expectation of success.

To this end, McLaughlin state the following:

> "Other dNTPs, such as deoxyuridine triphosphate ("dUTP"), and dNTP analogs [***which would be considered to be non-conventional nucleotides***], and conjugated dNTPs may also be used..." (column 6, lines 19-22; McLaughlin et al.)

> "Deoxynucleotide triphosphates ("dNTPs"), which are the building blocks of the amplification nucleic acid molecules, are typically supplied in standard PCR reactions at a concentration of 40-200 μM each ..." (column 6, lines 14-17) with contemplation of, "higher than 200 μM…" being advantageous (column 6, lines 25-26; McLaughlin et al.)

Provided that McLaughlin et al. explicitly state that the reagents employed by Mukai et al. (dNTPs including dUTPs in PCR reactions) are combinable and workable at the same ranges (40-200 μM each, and higher than 200 μM), one of ordinary skill in the art would have had no doubt that the combination of the teaching would have been successful.

As to the primers, wherein all the thymidines are completely replaced by uracil, such modification would have been obvious to one of ordinary skill in the art, for the purpose of generating amplicons which comprises all uracil bases in the amplified products.

Therefore, for the above reasons, the invention as claimed is *prima facie* obvious over the cited references.

Conclusion

No claims are allowed.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Young J. Kim whose telephone number is (571) 272-0785. The Examiner is on flex-time schedule and can best be reached from 6:00 a.m. to 2:30 p.m (M-F). The Examiner can also be reached via e-mail to Young.Kim@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Benzion, can be reached at (571) 272-0782.

Papers related to this application may be submitted to Art Unit 1637 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. All official documents must be sent

to the Official Tech Center Fax number: (571) 273-8300. For Unofficial documents, faxes can be sent directly to the Examiner at (571) 273-0785. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Young J. Kim/
Primary Examiner
Art Unit 1637
9/29/2009

/YJK/